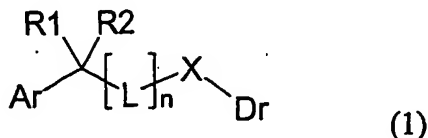


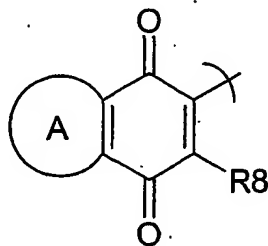
CLAIMS

1. A compound of formula (1), or a pharmaceutically acceptable salt thereof,

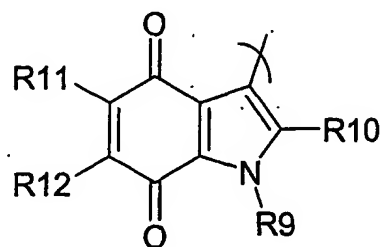


wherein:

- Ar is a substituted aryl or heteroaryl group bearing at least one nitro or azido group or is a group of formula (2) or (3)



(2)



(3)

- R_1 and R_2 , which may be the same or different are independently optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, aryl, COR_3 or, together with the intervening carbon atom, form an optionally substituted heterocycloalkyl or carbocyclic ring ;
- L is $-\text{OC}(\text{O})-$ or $-\text{OP}(\text{O})(\text{OR}_6)-$;
- n is 0 or 1;
- X is O, S, NR_7 or a single covalent bond;
- R_3 is OR_4 or NR_4R_5 ;
- R_4 , R_5 , R_6 and R_7 are each independently hydrogen or optionally substituted alkyl or,
- where R_3 is NR_4R_5 , R_4 and R_5 can be joined to form, together with the intervening nitrogen atom, a heterocycloalkyl ring;
- R_8 is hydrogen, alkoxy or dialkylaminoalkyl;

- R₉ is optionally substituted alkyl;
- R₁₀ is hydrogen, alkyl, alkoxy or dialkylaminoalkyl;
- R₁₁ and R₁₂ are independently hydrogen, alkyl, alkoxy, thioalkoxy, amino, alkylamino, dialkylamino, morpholino, piperidino, piperazino or 1-aziridinyl;
- 5 - A is an optionally substituted aryl or heteroaryl ring; and
- Dr is a moiety such that DrXH represents a cytotoxic or cytostatic compound.

2. A compound according to claim 1, wherein the alkyl, alkenyl and alkynyl groups in the R₁ to R₁₂ substituents are unsubstituted or substituted with 1, 2 or 3
10 unsubstituted substituents selected from halogen, amino, mono(C₁-C₄ alkyl)amino, di(C₁-C₄ alkyl)amino, hydroxy, C₁-C₄ alkoxy, C₁-C₄ alkylthio and (C₁-C₄ alkyl)sulphonyl groups.

3. A compound according to any one of the previous claims, wherein aryl and
15 heteroaryl groups in the Ar, A and R₁, R₂ substituents are unsubstituted or substituted with 1, 2 or 3 unsubstituted substituents selected from halogen, C₁-C₆ alkyl, hydroxy, amino, C₁-C₄ haloalkyl, C₁-C₄ alkoxy and C₁-C₄ haloalkoxy.

4. A compound according to any one of the previous claims, wherein the
20 heterocycloalkyl ring and carbocyclic rings in the R₁ to R₃ substituents are unsubstituted or substituted with 1, 2 or 3 unsubstituted substituents selected from halogen, C₁-C₆ alkyl, hydroxy, amino, C₁-C₄ haloalkyl, C₁-C₄ alkoxy and C₁-C₄ haloalkoxy.

25 5. A compound according to any one of the previous claims, wherein R₁ and R₂, together with the carbon to which they are attached, form a 3 to 10 membered heterocycloalkyl ring or a C₃₋₁₀ carbocyclic ring, which ring is unsubstituted or substituted by 1, 2 or 3 unsubstituted substituents selected from halogen, C₁-C₆ alkyl, hydroxy, amino, C₁-C₄ haloalkyl, C₁-C₄ alkoxy and C₁-C₄ haloalkoxy.

6. A compound according to claim 5, wherein R_1 and R_2 , together with the carbon to which they are attached, form a 5 to 6 membered heterocycloalkyl ring, which ring is unsubstituted or substituted by one unsubstituted C_1 - C_2 alkyl group.
- 5 7. A compound according to any one of claims 1 to 4, wherein R_1 and R_2 are the same or different and each represent unsubstituted C_1 - C_6 alkyl, unsubstituted C_1 - C_6 alkenyl, unsubstituted C_1 - C_6 alkynyl, a COR_3 group, an unsubstituted phenyl group or a phenyl group which is substituted with 1, 2 or 3 unsubstituted substituents selected from halogen, C_1 - C_6 alkyl, hydroxy, amino, C_1 - C_4 haloalkyl, C_1 - C_4 alkoxy
10 and C_1 - C_4 haloalkoxy.
8. A compound according to claim 7, wherein R_1 and R_2 are the same or different and each represent unsubstituted C_1 - C_4 alkyl, unsubstituted C_1 - C_4 alkenyl, unsubstituted C_1 - C_4 alkynyl, a COR_3 group, an unsubstituted phenyl group or a
15 phenyl group which is substituted with 1, 2 or 3 unsubstituted substituents selected from halogen, C_1 - C_4 alkyl, hydroxy, amino, C_1 - C_2 haloalkyl, C_1 - C_2 alkoxy and C_1 - C_2 haloalkoxy.
9. A compound according to claim 7 or 8, wherein R_3 is hydroxy, unsubstituted
20 C_1 - C_4 alkoxy or NR_4R_5 , wherein R_4 and R_5 are the same or different and each represent hydroxy or unsubstituted C_1 - C_4 alkoxy, or R_4 and R_5 form, together with the nitrogen atom to which they are attached, a 3 to 10 membered heterocycloalkyl ring, which ring is unsubstituted or substituted by 1, 2 or 3 unsubstituted substituents selected from halogen, C_1 - C_6 alkyl, hydroxy, amino, C_1 - C_4 haloalkyl, C_1 - C_4 alkoxy
25 and C_1 - C_4 haloalkoxy.
10. A compound according to claim 9, wherein R_3 is hydroxy, unsubstituted C_1 - C_2 alkoxy or NR_4R_5 , wherein R_4 and R_5 are the same or different and each represent hydrogen or unsubstituted C_1 - C_4 alkyl.

11. A compound according to any one of claims 7 to 10, wherein R_1 and R_2 are the same or different and each represent unsubstituted C_1 - C_2 alkyl or an unsubstituted $-CO_2$ -(C_1 - C_2 alkyl) group.
- 5 12. A compound according to any one of the preceding claims wherein n is 0 and X is O or S.
13. A compound according to any one of claims 1 to 11, wherein n is 1 and X is NH.
- 10 14. A compound according to any one of claims 1 to 11 or 13, wherein n is 1 and L is $-OC(O)-$ or $-OP(O)(OR_6)$, wherein R_6 is hydrogen or unsubstituted C_{1-6} alkyl.
- 15 15. A compound according to claim 14, wherein L is $-OC(O)-$.
16. A compound according to any one of the previous claims, wherein Ar is a substituted aryl or heteroaryl group, which group carries one substituent selected from nitro and azido substituents and 0, 1 or 2 further unsubstituted substituents chosen from halogen, C_1 - C_6 alkyl, hydroxy, amino, C_1 - C_4 haloalkyl, C_1 - C_4 alkoxy and C_1 - C_4 haloalkoxy substituents .
- 20 17. A compound according to claim 16, wherein Ar is a phenyl group or a 5- or 6-membered heteroaryl group, which group carries only one substituent which substituent is selected from nitro and azido substituents.
- 25 18. A compound according to claim 17, wherein Ar is an unsubstituted group selected from nitrophenyl, nitroimidazole, nitrothiophene and nitrofuranyl groups.
- 30 19. A compound according to any one of the previous claims, wherein $DrXH$ is selected from an anthracyclin antibiotic, an antimetabolite, a topoisomerase inhibitor, an inhibitor of mitosis, inhibitors of protein kinases and an antagonist of (6 R)-5,6,7,8-tetrahydrobiopterin.

20. A compound according to claim 19, wherein DrXH is selected from doxorubicin, epirubicin, daunorubicin, 5-fluorouracil, 6-mercaptopurine, 6-thioguanine, cytarabine, gemcitabine, capecitabine, fludarabine, cladribine, 5 decitabine (5-aza-2'-deoxycytidine), troxacitabine (2'-deoxy-3'-oxacytidine), 5-azacytidine, 4'-thioaracytidine, tezacitabine, clofarabine, trimetrexate and methotrexate, etoposide and teniposide, topotecan, SN38, combretastatin A4, combretastatin A1, podophyllotoxin, vinblastine, vincristine, vinorelbine, paclitaxel and docetaxel, an epothilone, deoxyepothilone B BMS 247550, a dolastatin 10 derivative, a cryptophycin derivative, gefitinib, erlotinib, ZD6474 and AZD2171.
21. A compound according to claim 20, wherein DrXH is combretastatin A4, etoposide, cytarabine or 6-mercaptopurine.
- 15 22. A compound according to any one of the previous claims which is 1-(4-Methoxy-3-(2-(5-nitrothiophen-2-yl)propan-2-yl)oxyphenyl-2-(3,4,5-trimethoxy)phenyl-Z-ethene, 1-(4-Methoxy-3-(2-(4-nitrophenyl)propan-2-yl)oxyphenyl-2-(3,4,5-trimethoxy)phenyl-Z-ethene, 9-(7,8-Dihydroxy-2-methyl-hexahydro-pyrano[3,2-d][1,3]-dioxin-6-yloxy)-5-{3,5-dimethoxy-4-[1-methyl-1-(4-nitrophenyl)ethoxy]-phenyl}-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho[2,3-d][1,3]dioxol-6-one, 6-(2-(4-nitrophenyl)propan-2-ylsulfanyl)-9H-purine, 1-(4-Methoxy-3-(1-methyl-4-(5-nitrothien-2-yl)piperidin-4-yl)oxycarbonyloxy)phenyl-2-(3,4,5-trimethoxy)phenyl-Z-ethene, 1-(4-Methoxy-3-(2-(1-methyl-2-nitroimidazol-5-yl)propan-2-yl)oxyphenyl-2-(3,4,5-trimethoxy)phenyl- 20 Z-ethene, 6-(2-(5-nitrothien-2-yl)propan-2-ylsulfanyl)-9H-purine, N⁴-(2-(5-nitrothien-2-yl)prop-2-yl)oxycarbonyl-1-β-D-arabinofuranosylcytosine, 1-(3-(1-Ethoxycarbonyl-1-(5-nitrothien-2-yl)ethoxy)-4-methoxy-phenyl)-2-(3,4,5-trimethoxyphenyl)-Z-ethene and N-(2-{3-[1-Methyl-1-(5-nitrothiophen-2-yl)ethoxy]-phenyl}-ethyl)-acetamide, or a pharmaceutically acceptable salt thereof.

23. A pharmaceutical composition comprising a compound according to any one of the previous claims, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.
- 5 24. A compound according to any one of claims 1 to 22, or a pharmaceutically acceptable salt thereof, for use in the treatment of the human or animal body.
25. Use of a compound as defined according to any one of claims 1 to 22, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the
10 prevention or treatment of a proliferative disorder.
26. Use according to claim 25, wherein the proliferative disorder is cancer, rheumatoid arthritis, psoriatic lesions, diabetic retinopathy or wet age-related macular degeneration.
15
27. Use according to claim 25 or 26, wherein the proliferative disorder is a hypoxic disorder.
28. Use according to any one of claims 25 to 28, wherein the medicament is for
20 use in the prevention or treatment of a solid tumour or leukaemia.
29. A method of ameliorating or reducing the incidence of a proliferative disorder as defined according to any one of claims 25 to 28 in a patient, which method comprises administering to said patient an effective amount of a compound as
25 defined in any one of claims 1 to 22, or a pharmaceutically acceptable salt thereof.
30. A method according to claim 29, which method comprises administering to said patient an effective amount of
- (a) a compound as defined in any one of claims 1 to 22, or a pharmaceutically
30 acceptable salt thereof; and
- (b) a reductase, an anti-body reductase conjugate, a macromolecule-reductase conjugate or DNA encoding a reductase gene.

31. A product containing
- (a) a compound as defined in any one of claims 1 to 22, or a pharmaceutically acceptable salt thereof; and
 - 5 (b) a reductase, an anti-body reductase conjugate, a macromolecule-reductase conjugate or DNA encoding a reductase gene for the simultaneous, separate or sequential use in the treatment of a proliferative disorder as defined in any one of claims 25 to 28.